

## **IN THE CLAIMS**

1-31. (canceled)

32. (currently amended) An array of probes on a solid support for detecting gene expression, wherein at least one probe comprises at least ~~18~~ 44 contiguous nucleotides of SEQ ID NO:71 (NORF 5) ~~an open reading frame of a *Saccharomyces cerevisiae* genome, wherein the *Saccharomyces cerevisiae* genome is shown in SEQ ID NOS:12,204-12,219, wherein the open reading frame is selected from the group consisting of the open reading frames identified by the SAGE tags shown in SEQ ID NO:67 (NORF 1), SEQ ID NO:68 (NORF 2), SEQ ID NO: 70 (NORF 4), SEQ ID NO: 71 (NORF 5), SEQ ID NO: 72 (NORF 6), SEQ ID NO: 83 (NORF 17), SEQ ID NO:91 (NORF 25), and SEQ ID NO:93 (NORF 27).~~

33-34. (canceled)

35. (previously amended) The array of claim 32 which comprises at least 100 probes, wherein each probe has a sequence that is different from each other sequence.

36. (previously amended) The array of claim 32 which comprises at least 500 probes, wherein each probe has a sequence that is different from each other sequence.

37. (previously amended) The array of claim 32 which comprises at least 1,000 probes, wherein each probe has a sequence that is different from each other sequence.

43-44. (canceled)

45. (new) An array of probes on a solid support for detecting gene expression, wherein at least one probe consists of at least 18 contiguous nucleotides of SEQ ID NO:71 (NORF 5).

46. (new) The array of probes of claim 45 which comprises at least 100 probes, wherein each probe has a sequence that is different from each other sequence.

47. (new) The array of probes of claim 45 which comprises at least 500 probes, wherein each probe has a sequence that is different from each other sequence.

48. (new) The array of probes of claim 45 which comprises at least 1,000 probes, wherein each probe has a sequence that is different from each other sequence.

49. (new) The array of probes of claim 45 wherein the at least one probe consists of at least 25 contiguous nucleotides of SEQ ID NO:71 (NORF 5).

50. (new) The array of probes of claim 32 wherein the at least one probe comprises at least 25 contiguous nucleotides of SEQ ID NO:71 (NORF 5).

## **Remarks**

### The Amendments

Claim 32 has been amended to recite at least one probe that comprises at least 18 contiguous nucleotides of SEQ ID NO:71 (NORF 5). New claim 50 recites that the at least one probe comprises at least 25 contiguous nucleotides. New claims 45-49 parallel claims 32, 35-37, and 50 except that the recited at least one probe “consists of” at least 18 contiguous nucleotides of SEQ ID NO:71 (NORF 5). Probes of at least 18 or at least 25 contiguous nucleotides of a NORF are disclosed on page 8, lines 15-18: “Probes according to the present invention are isolated DNA molecules which have at least 10, and preferably at least 12, 14, 16, 18, 20, or 25 contiguous nucleotides of a particular NORF gene or other differentially expressed gene.”

None of these amendments introduces new matter.

### The Rejection of Claims 32, 35-37, 43, and 44 Under 35 U.S.C. § 101

Claims 32, 35-37, 43, and 44 stand rejected under 35 U.S.C. § 101 as lacking patentable utility. Claims 43 and 44 have been canceled. Applicants respectfully traverse the rejection of claims 32 and 35-37.

The Final Office Action maintains that claims 32 and 35-37 lack patentable utility for reasons stated in the Office Action mailed July 29, 2002. First, the July 29 Office Action asserted that “the application does not disclose that each of the NORFs identified by the SAGE tags mentioned in the claims is indeed differentially expressed during the cell cycle.” (Paper 18, page 2 lines 10-11.) To advance prosecution, independent claim 32 has been amended to recite one particular open reading frame (ORF), *i.e.*, NORF 5. The specification explicitly teaches that

this NORF is differentially expressed: “Genes which have been found to have differential expression characteristics include: NORF N<sup>o</sup> 1, 2, 4, 5, 6, 17, 25, 27. . . .” (Page 6, line 31.) Thus, amended claim 32 recites a NORF that is disclosed as differentially expressed during the cell cycle. New claims 45-50 also recite SEQ ID NO:71 (NORF 5).

Second, the July 29 Office Action asserted that the claims lack patentable utility because “it does not necessarily follow that each of the 14-mers contained in each of the so-identified NORFs is found only in DNAs that are differentially expressed during the cell cycle.” (Paper 18, page 2, lines 14-16.) Independent claim 32 has been amended to recite “at least one probe [that] comprises at least 18 contiguous nucleotides of SEQ ID NO:71 (NORF 5).” New independent claim 45 recites “at least one probe [that] consists of at least 18 contiguous nucleotides of SEQ ID NO:71 (NORF 5).” As demonstrated below, a probe of at least 18 contiguous nucleotides of NORF 5 is long enough to identify NORF 5 and nothing else in the *Saccharomyces cerevisiae* genome.

A compact disc accompanies this amendment. The compact disc contains one file that lists all 191 possible 18-mers contained within the open reading frame identified as NORF 5 and shown in SEQ ID NO:71. The compact disc also contains 16 files that contain the original, unfiltered results of “batch blasts” of all the NORF 5 18-mers carried out against each of the 16 *Saccharomyces cerevisiae* chromosomes shown in SEQ ID NOS:12,204-12,219. The searches were carried out using “primer mapping” tools available on the website [http://sky.bsd.uchicago.edu/primer\\_compact.htm](http://sky.bsd.uchicago.edu/primer_compact.htm). The results are submitted on a compact disc because, if printed, the files would total thousands of pages.

NORF 5 is located on chromosome 13. See Table 3 on page 23 of the specification. Consistent with this location, the file on the compact disc identified as “NORF 5 18-mers vs chromosome 13” shows a single exact match for each of the 191 possible 18-mers. In contrast, none of the batch blasts of the NORF 5 18-mers carried out against any of chromosomes 1-12, 14, or 16 shows any match of 18 identical nucleotides. Thus, a probe of at least 18 contiguous nucleotides of NORF 5 is sufficiently long to uniquely identify NORF 5 (*i.e.*, a gene that is differentially expressed during the cell cycle) in the *Saccharomyces cerevisiae* genome.

Applicants respectfully request withdrawal of this rejection.

The Rejection of Claims 32, 35-37, 43, and 44 Under 35 U.S.C. § 112, second paragraph

Claims 32, 35-37, 43, and 44 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Claims 43 and 44 have been canceled. Applicants respectfully traverse the rejection of claims 32 and 35-37.

The second paragraph of 35 U.S.C. § 112 states that:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

It is well settled that a claim must “reasonably apprise those skilled in the art both of the utilization and scope of the invention.” *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 134-38, 118 U.S.P.Q. 122, 130 (2d Cir. 1958), *cert. denied*, 358 U.S. 884 (1958). Claims 32 and 35-37, as well as new claims 45-50, meet this standard.

The Final Office Action asserts that the claims “do not identify with particularity the sequences claimed.” Page 2, third paragraph. Amended independent claim 32 is directed to an

array of probes on a solid support for detecting gene expression, wherein at least one probe comprises at least 18 contiguous nucleotides of SEQ ID NO:71 (NORF 5). New independent claim 45 is directed to an array of probes on a solid support for detecting gene expression, wherein at least one probe consists of at least 18 contiguous nucleotides of SEQ ID NO:71 (NORF 5). SEQ ID NO:71 is provided in the sequence listing. It would be a simple matter for those skilled in the art to determine whether or not any given probe comprises or consists of at least 18 contiguous nucleotides of SEQ ID NO:71; thus, it would be clear whether or not any given probe falls within the scope of claims 32, 35-37, or 45-50. Each of claims 32, 35-37, and 45-50 identifies with particularity the sequences of the recited probes. Thus, each of these claims is definite.

Applicants respectfully request withdrawal of this rejection.

The Rejection of Claims 32, 35-37, 43, and 44 Under 35 U.S.C. § 103(a)

Claims 32, 35-37, 43, and 44 stand rejected under 35 U.S.C. § 103(a) as obvious over Goffeau *et al.*, *Science* 270, 546, October 25, 1996 (“Goffeau”) in view of Velculescu *et al.*, *Science* 274, 484, October 20, 1995 (“Velculescu”). Claims 43 and 44 have been canceled. Applicants respectfully traverse the rejection of claims 32 and 35-37. The arguments below apply with equal force to new claims 45-50.

The U.S. Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of obviousness. The *prima facie* case requires three showings:

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a

reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations.

Manual of Patent Examining Procedure, 8<sup>th</sup> ed., § 2142.

Goffeau is cited as teaching “the fact that the entire genome of *Saccharomyces cerevisiae* is known.” Paper 7, page 7, lines 7-8. Velculescu is cited as teaching “the analysis of DNA by attaching DNA probes to a solid support.” Paper 7, page 7, lines 8-9. The U.S. Patent and Trademark Office has taken the position “the broad motivation of analysis of *Saccharomyces* DNA is sufficient to establish obviousness under 35 U.S.C, § 103(a).” Paper 18, page 3, lines 5-6. This motivation, however, is legally insufficient to support a *prima facie* case of obviousness.

The asserted motivation is a purely academic or philosophical goal leading to no particular practical result. While this may be sufficient motivation to undertake an academic plan of research, this is not a sufficient motivation according to the patent law. The Court of Customs and Patent Appeals in *In re Stemniski* denigrates “abstract, theoretical, or academic considerations.” 170 U.S.P.Q. (BNA) 343, 347 (C.C.P.A. 1971). The court looked to

practical considerations which promote the progress of the useful arts or are of use to society . . . . Where the prior art reference neither discloses nor suggests a utility for certain described compounds, why should it be said that a reference makes obvious to one of ordinary skill in the art an isomer, homolog or analog of related structure, when that mythical, but intensely practical, person knows of no “practical” reason to make the reference compounds, much less any structurally related compounds?

*Id.* No practical or real world utility was known or postulated for the open reading frame recited in independent claims 32 and 45 (*i.e.*, NORF 5). In fact, no utility at all was known for this open reading frame, because it was not even recognized to exist. The claimed arrays could not have been obvious when no utility was known for the recited probe.

One of skill in the art does not “analyze” in a vacuum. One of skill in the art analyzes for a reason. No reason exists in the prior art that would have motivated one of ordinary skill in the art to make the claimed array.

There are a limited number of reasons for analyzing nucleic acids: nucleic acids can be analyzed to determine their nucleotide sequence, their expression levels, their expression in different tissues, or what they encode. Of course, because Goffeau discloses the entire nucleotide sequence of the *S. cerevisiae* genome, there would have been no motivation to determine the sequence again.

This leaves as possibilities for analysis either determination of levels or patterns of gene expression in tissues or identification of the encoded products. As to identification of encoded products, Applicants acknowledge that Goffeau teaches that “one of the major problems to be tackled during the next stage of the yeast genome project is to elucidate the biological functions of all these genes.” Page 546, lines 6-9 of the Abstract. This statement, however, would not have provided any motivation to attach the recited probes to a solid support in an array. Before this application was filed, the NORF identified by the recited probes was not known to be an expressed gene. The open reading frames, which Applicants refer to as “NORFs,” (“not previously assigned open reading frames,” page 6, line 20) are disclosed only in the present specification, not in the cited prior art. Thus, neither Goffeau nor Velculescu could possibly



have provided any teaching or suggestion that would have motivated one of ordinary skill in the art to identify NORF 5's expressed products. NORF 5 was simply not known to be an expressed gene.

The only "analysis" remaining and, indeed, the only purpose for which one of ordinary skill in the art would have attached probes to a solid support in an array, is to analyze expression patterns in tissues or levels of gene expression by hybridizing mRNA to the probes. Without any teaching in either Goffeau or Velculescu that the recited NORF is expressed, however, there would have been no reason to attach the recited probes to a solid support in an array to detect NORF 5 expression. Without this teaching --present only in Applicants' specification-- such an array would have had no known utility whatsoever and no ordinary artisan would have been motivated to make it.

The Final Office Action mailed June 11, 2001 asserted that because the claims recite that the probes comprise at least 14 contiguous nucleotides of a NORF gene, "there is no need for the references to disclose any of the ORFs mentioned in the application." Paper 11, page 3, lines 8-9. That is, the U.S. Patent and Trademark Office asserts that one of ordinary skill in the art would have been motivated to use probes long enough to encompass nucleotides both of a known expressed gene to be analyzed and of a region of the *S. cerevisiae* genome not thought to be expressed (*i.e.*, a probe would comprise the 14 contiguous nucleotides of NORF 5 and all intervening sequences between NORF 5 and the known gene). This, however, is not true. One of ordinary skill in the art would not have been motivated to use such a probe to detect gene expression. On the contrary, to minimize non-specific hybridization, one of ordinary skill in the art would have been motivated to use a probe that hybridizes only to the nucleotide sequence of


the known gene. In any event, the Office's assertion does not apply to new claims 45-49, each of which recites that at least one probe *consists of* at least 18 contiguous nucleotides of SEQ ID NO:71 (NORF 5).

There simply is no teaching in the cited references or in the patent application sufficient to have motivated one of ordinary skill to have attached the recited probes to a solid support in an array.

Applicants respectfully request withdrawal of this rejection.

Respectfully submitted,  
BANNER & WITCOFF, Ltd.

Date: October 1, 2003

By:   
Lisa M. Hemmendinger  
Registration No. 42,653

1001 G Street, N.W.  
Eleventh Floor  
Washington, D.C. 20001-4597  
(202) 824-3291